REMARKS

Claims 1-29 were finally rejected in an Office Action mailed September 23, 2002 (Paper 8). On appeal, the Board of Patent Appeals and Interferences remanded the case for further examination, with certain observations and remarks regarding the merits of the applicant's and the examiner's arguments, and on the patentability of the claimed subject matter, made "in an effort to advance prosecution." Remand, page 6. The examiner has nonetheless maintained his prior rejections of all of the pending claims in an Office Action mailed October 12, 2005, without reference to the Board's observations beyond merely noting the fact of the Remand (see page 2), and indeed apparently without taking them into account at all. In the present amendment the applicant cancels claims 1-3, 15-18 and 24-29, adds new claims 30 and 31, and amends claims 4, 6, 8-11, 13, 14, 19 and 20, which the applicant believes addresses all of the points raised by the Board, and overcomes the pending rejections. Claims 4-14, 19-23, 30 and 31 are presently pending in this application.

Support for new claim 30 is found throughout the specification, for example at, *inter alia*, page 5, line 29 to page 6, line 2, page 6, lines 24-30, page 9, lines 5-14 and lines 26-29, page 10, lines 25-26, page 20, lines 2-6 and throughout Comparative Example 1/B (page 20, line 1 to page 21, line 26), in Comparative Example 1/C (page 21, line 26 to page 22, line 10) and at page 26, lines 25-30. Support for new claim 31 is likewise found throughout the specification, for example at the pages cited above, and also at page 7, lines 2-25, and page 29, lines 10-22.

Claims 4, 6, 8, 10, 11, 13, 14, 19 and 20 have been amended to change their dependency from canceled claim 1 to new claim 30.

Claims 6, 8, 9, 11 and 19 are amended in order to provide consistency in the use of the plural, and reference to antecedent basis, throughout the claims. Claim 13 is amended to correct a typographical error (omission of a "degree" sign). Claim 20 is amended in order to adjust the designation of the recited process steps to correspond to the equivalent steps in new claim 30, from which it now depends.

No new matter is added by these amendments.

I. NON-STATUTORY DOUBLE PATENTING

The Patent Office has rejected all of the pending claims for non-statutory ("obviousness-type") double patenting. Final Office Action, pages 3-4. The Patent Office Asserts that the rejected claims are unpatentable over claims 1-14 of U.S. Patent No. 6,022,730. The applicant provides herewith a terminal disclaimer over the term of U.S. Patent No. 6,022,730, thus overcoming this rejection.

II. REJECTION UNDER § 101.

Claims 1-29 were rejected under 35 U.S.C. § 101 for lack of utility. The cancellation of claims 1-3, 15-18 and 24-29 makes this rejection moot with respect to those claims.

The examiner has maintained this rejection despite the Board's clear statements that this rejection was without merit. The examiner continues to argue that the claims are directed to methods for the "spontaneous generation," or creation, of new life. October 12, 2005 Office Action, page 7. As a first matter, the examiner is incorrect in equating "de novo speciation" with "creation of life." *C.f.*, *id.* The former refers to the development or formation of a new *species*, while the latter means to formation of a living thing from lifeless matter. Even the definitions quoted by the examiner make this clear.

The examiner asserts that "[c]ontrary to Applicant's assertion, none of the evidence presented demonstrate [sic] the operability of the claimed invention." October 12, 2005 Office Action, page 7. However, in its remarks on remanding this case, the Board acknowledged that the record supported Applicant's arguments made at pages 8-9 of the Appeal Brief, and at page two of the Reply, that the claimed process, when practiced under sterile conditions, starts with cells identifiable as belonging to or coming from one species (a eukaryotic cell), and "resulted in the 'production'" of cells that are identifiable as belonging to another (a bacterium), or stated differently "*de novo* speciation." Remand, pages 7-8.[1] The examiner has not framed this rejection in terms of a lack in the claims of a limitation requiring that sterile conditions be maintained throughout the process, but rather in terms of the inherent inoperability of a method for the "creation of life." Thus, the examiner's position directly contradicts that taken by the Board, and does not "advance prosecution," as the Board intended its observations on remand to do. The Board, in fact, was "unable to identify any evidence upon which the examiner relies upon to support [the examiner's] assertion." Remand, page 9. Neither did the Board find "evidence on this record to explain why these 'strains of bacteria' would contaminate cells cultured under sterile conditions, and even if they did why these 'strains of bacteria' would contain a eukaryotic and/or viral gene as required by the appellant's claimed invention." *Id.* It is

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[1] The Board noted that the evidence of record supported this argument, by stating that "[w]ith regard to the term 'identifiable' we note that according to the Steuer Declaration (paragraph 4), notwithstanding rigorously sterile conditions, the claimed method results in the 'production' of bacteria identified as *B. licheniformis*." Remand, page 8.

thus evident that the Board agrees with the applicant that the claimed method, when practiced under sterile conditions, produces from a eukaryotic cell line a cell identifiable as a bacterium, and that there is no record evidence to the contrary. Applicant notes that it is apparent from the Board's use of the terms "producing" and "production" in its remarks describing the invention, that the Board considers these terms to be appropriate for use in describing the nature of the process, and as used in the context of the claims does not mean that the applicant is claiming "creation of life."

The Board, however, pointed out that the claims recite production of a "bacterium," not of a cell identifiable as a bacterium, and did not recite that the starting eukaryotic cell culture is uncontaminated by bacteria. *Id.* In view of the Board's remarks, the applicant has canceled independent claims 1 and 24, and added new independent claims 30 and 31, which expressly require that the starting eukaryotic cell culture be free of overt microbial contamination (*i.e.*, sterile), and that sterile conditions be maintained throughout each process step. The remaining pending claims all depend from either claim 30 or claim 31, and thus include all of the limitations of those claims. Claim 30 also includes a final step (f) of identifying "a cell that is identifiable as a bacteria, and contains a eukaryotic and/or viral gene," language suggested by the Board to describe the invention. Applicant believes that new claims 30 and 31 recite the invention in a manner which addresses the issues noted by the Board with regard to the issue of contamination by (a) requiring that sterile conditions be maintained throughout the process in order to assure that the resulting cell line is not the result of overt bacterial contamination, and (b) expressly reciting the features that characterize the cell line produced as being distinct from the cells of the starting eukaryotic cell culture. Applicant therefore believes that new claim 30, from which pending claims 4-14, 19-23 depend, either directly or indirectly, and new claim 31, from which claim 27 depends, describe the invention in terms that make clear that what is being claimed is not a method for "spontaneous generation," or creation, of life, and that the invention as claimed has a credible utility. Applicant therefore submits that the rejection under § 101 does not apply to new claims 30 and 31, nor to claims 4-14 and 19-23 depending therefrom. Applicant therefor respectfully requests that the rejection of claims 4-14 and 19-23 under § 101 be withdrawn, and that this rejection not be applied to new claims 30 and 31.

III. REJECTIONS UNDER § 112.

A. Rejections Under § 112, first paragraph.

1. Enablement (deposit requirement)

The examiner continues to argue that a deposit is necessary in order to meet the requirements of § 112, 1st paragraph. The Board unambiguously stated in its Remand that because no claim requires a specific cell line, the issue was actually an objection to the specification and *not* a claim rejection. Remand, page 3. Nonetheless, the examiner has maintained this as a claim rejection. October 12, 2005 Office Action, pages 8-9. Because none of the pending claims require a specific cell line, a deposit, and the accompanying certification and amendments to the specification, are not be required as a condition of the patentability of any pending claim.[2] Applicant therefor submits that, as pointed out by the Board in its observations on Remand, this rejection is improper.

Furthermore, with regard to any asserted enablement-related issue with the specification, Applicant again notes that a number of cell lines suitable for use in the claimed invention, including those used in the working examples of the specification, are in fact publicly available. *C.f.*, specification, page 8. The examiner asserts that there is no enablement beyond methods using the specific starting cell lines, to produce the specific product cells lines, of the examples. However, "[t]he enablement requirement is met if the description enables any mode of making and using the claimed invention." *Engel Indust., Inc. v. Lockformer Co.*, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). The practice of the claimed methods does *not* require a specific cell line as starting material. Rather, the claims require the use of "a culture of virally-infected eukaryotic cells." The specification states that suitable virally infected eukaryotic cells can be obtained from a variety of sources, including the American Type Culture Collection

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[2] In any event, Applicant points out that the specification states that the cell lines used in the working examples of the specification have, in fact, been deposited with the ATCC, and provided the deposit accession numbers in a table located at page 8 of the specification. The deposit certificates for these cell lines have already been provided to the Patent Office, along with the required certifications, in the parent case, Ser. No. 08/719,367, now U.S. Patent 6,022,703, which forms a part of the record of this case. The examiner, therefore, is incorrect in his assertion at page 9 of the October 12, 2005 Office Action that the requirements of the Budapest Treaty have not been met. Copies of these deposit certificates and certification are annexed to this filing for the examiner's convenience (the certification of compliance for ATCC 11655 appears at page 4 of the applicant's September 25, 1996 Amendment).

(ATCC), and furthermore provides guidance in the form of a literature reference as to how to prepare other suitable new virally infected eukaryotic cells. Specification, page 9, line 26 to page 10, line 2. The specification also identifies by name and ATCC accession number three such suitable cell lines (ATCC CRL 11655, ATCC CRL 1807, ATCC HTB 38 and ATCC HT-29), the public availability of which prior to the priority date of the present application is a matter of public record (*see*, *e.g.*, deposit certificate for ATCC CRL 11655, a copy of which is attached for the examiner's convenience). Specification, page 22, lines 20-22; page 28, lines 2-11.

The Federal Circuit has opined on precisely this issue:

> [n]o deposit is necessary if the biological organisms can be obtained from readily available sources or derived from readily available starting materials through routine screening that does not require undue experimentation.

In re Wands, 858 F.2d 731, 736 (Fed. Cir. 1988). In the present case starting materials for the claimed methods can be obtained both from readily available sources (such as the ATCC) and by routine experimentation, applying, for example, the methods disclosed in the specification and the references cited therein. The applicant therefore submits that there can be no issue of enablement that requires a cell deposit by the applicant, and also for this reason requests that this rejection be withdrawn.

2. Enablement (rejection of claims 1-29)

Claims 1-29 also have been rejected under § 112, 1st paragraph, for lack of enablement. The examiner asserts that while the specification enables a method for *isolating* a bacterium, it does not enable *production* of a bacterium. October 12, 2005 Office Action, pages 10-11. The cancellation of claims 1-3, 15-18 and 24-29 makes this rejection moot with respect to those claims. For reasons unrelated to this rejection, the remaining claims are amended such that they no longer include the terms "production" or "producing," making this rejection also moot as to the remaining claims. It should be noted, however, that it is evident from its observations on remand that the Board has accepted the term "production" as appropriate for describing the invention, *i.e.*, that its use does not refer to spontaneous generation, or creation, of life, (*see* Remand, pages 7-8), and further that the evidence of record shows that the specification does, in fact, enable the production of a cell identifiable as a bacterium from a sterile culture of virally-infected eukaryotic cells. *See* Remand, pages 8-9. Thus, the examiner's insistence on maintaining this rejection based on the alleged lack of enablement of the "production" of a new

line, as opposed to the "isolation" of such a cell line, has been specifically found to be without merit by the Board.

The examiner, however, now also asserts that the specification does not even enable the "isolation" of any cell lines other than the ones specifically identified in the specification. Despite being specifically directed by the Board to support his findings of fact and conclusions of law with "*substantial evidence within the record* " (Remand, pages 9-10, italics added), the examiner fails to provide any evidentiary support for his position, or point to any evidence in the record to support the assertion that the specification enables the isolation only of the specific cell lines produced in the working examples. On the contrary, the evidence of record, including the Steuer Declaration, the Robinson Declaration, and the Final Report attached to the Robinson Declaration, establishes within a reasonable degree of scientific certainty that the claimed methods are enabled. The examiner maintains that the evidence of record doe not rule out the possibility of contamination: "it is unclear that the claimed method would be suitable for the recovery of any and all bacteria, a few of which may be present, but not detectable by certain means;" "one of ordinary skill in the art would not reasonably expect any and all possible viral infected eukaryotic cell cultures to harbor or to be contaminated by bacteria;" "it is unclear what precautions were taken in the instant case to assure that the bacteria harvested are not incidental contaminants in advertently introduced into the cell culture." However, Dr. Steuer, in his September 30, 1997 Declaration, *expressly* addresses this issue:

> 5. I have read portions of an Office Action issued by the Patent and Trademark Office, The portions I read comments upon the attached Final Report, which I understand was previously submitted with a Declaration by Dr. Robinson. In paragraph no. 16, the Office Action states that the Final Report did not "rule our the possibility of bacterial contamination at each and every step of the claimed method." The Office Action therefore expresses the view that the results were due to contamination. I disagree with both that conclusion and the reasoning behind it that is presented in the Office Action.
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> 7. The Final Report provides extensive details regarding the specific sterility testing and aseptic cell culturing techniques that were employed. Addition verification of the quality of this work is provided on page 33 of the Final Report.
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8. It is my professional opinion that any scientific inquiry wherein one must "rule out" contamination, as set forth in the Office Action, is meaningless. Scientists in this field do not "rule out" contamination. This is why the Final Report states that "the possibility of environmental contamination as the source of the bacterial isolates cannot be absolutely eliminated." For this same reason I worded my conclusion that contamination "was highly unlikely. No scientist skilled in the field would state that the possibility of contamination had been "absolutely eliminated: or "ruled out" in any scientific procedure such as this. Rather, procedures are carried out under rigorously-controlled aseptic environments that minimize the possibility of contamination. The equipment, materials and procedures used at my company to test starting materials for contamination, and that were used in connection with Dr. Robinson's work, are recognized as meeting the highest quality standards. Thus, I concluded that the Patent Examiner has applied a requirement for "proving" a lack of contamination that is not applied by persons skilled in this field.

The examiner has ignored this unimpeached evidence in the record, or simply dismissed it as lacking sufficient credibility. Nor is this evidence applicable merely to the specific experiments performed under Dr. Steuer's supervision, as he unambiguously states that the methods "used in connection with Dr. Robinson's work" also met the accepted scientific standards he describes. The examiner has provided not one piece of evidence that rebuts or impeaches Dr. Steuer's Declaration.[3] The Patent Office cannot simply discount an applicant's statements supporting enablement by requiring "greater scientific precision than did any of the scientists whose testimony [is] presented." *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1575 (Fed. Cir. 1991). In *Scripps* the Federal Circuit, noting that § 112 "is directed to persons of skill in the field of the invention," held that it was reversible error for the lower court to find a lack of enablement where there was "no evidence that one skilled in the field of this invention could not make and use a product satisfying all the limitations of the claims, by

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[3] The only evidence that the examiner has put in the record is an excerpt from a book that states that microbial contamination of cell culture is a common occurrence. It does *not* establish that cell cultures that are found to be free of any microbial contamination under the accepted scientific standards in the field are still considered by workers in the field to be contaminated, nor does it establish that microbial contamination is a universal or inevitable phenomenon is the field of cell culture.

following the inventors' disclosure and the knowledge of the art." *Id.* In the present case, the evidence of record establishes that it is possible for one skilled in the art to successfully practice the claimed invention. There is no evidence in the record to the contrary, much less the substantial evidence that is required.

It is long settled by the courts that an applicant simply is not required to disclose every species within the scope of the claims, even in an "unpredictable" art. *See, e.g., In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1990); *see also In re Angstadt & Griffin*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976); MPEP, § 2164.02 ("Because only an enabling disclosure is required, applicant need not describe all actual embodiments."). Nor is an applicant required to test all the embodiments of the invention. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991) (citing *Angstadt*). The question thus is whether or not the specification provides sufficient guidance to the person of ordinary skill in the art to practice the invention throughout its scope without resort to undue experimentation. Under the proper standard, even a considerable amount of experimentation is not "undue" in the context of § 112, 1st paragraph, if that experimentation is routine, and in particular when one skilled in the art would know how to determine, using established methods, which embodiments are operative and which are not. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984). The Federal Circuit has noted that

> The Patent and Trademark Office Board of Appeals summarized the point well when it stated:
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> > The test is not merely quantitative, since a *considerable amount* of experimentation is permissible, if it is merely routine, or if the specification in question provides a *reasonable amount of guidance* with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

PPG Indust., Inc. v. Guardian Indust. Corp., 73 F.3d 1558, 1564 (Fed. Cir. 1996) (citing *Ex. Parte Jackson*, 217 U.S.P.Q. 804, 807 (BPA 1982)) (emphasis added). For example, in *Wands* the Federal Circuit found that a claim covering a general class of monoclonal antibody-based assay methods did not lack enablement, because a person using the state of the art and the specification disclosure, could produce and screen new hybridomas to determine if they secreted antibodies falling within the claimed class, without undue experimentation. 858 F.2d at 736-37 ("enablement is not precluded by the necessity form some experimentation such as routine screening [to identify hybridomas that secrete the desired antibody]...").

The case of *Ajinomoto Co., Inc. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338 (Fed. Cir. 2000) is particularly applicable in the present case. In *Ajinomoto* the Federal Circuit held that a claim to a method of genetically modifying a bacterium via directed mutation to produce an amino acid was enabled, because all of the methods needed to practice the invention were known in the art. The Federal Circuit approved of the lower court's finding that

> [d]espite the diversity existing among bacteria, practitioners of this are were prepared to carry out the identification, isolation, recombination and transformation steps required to practice the full scope of the claims.

Ajinomoto, 228 F.3d at 1345 The same fact pattern exists in the present case: the method steps of selecting starting materials, performing the recited culture steps, and characterization and identification of the cell produced thereby, are all within the ordinary skill in the art. The examiner has provided no evidence to refute this. What is more, the specification provides detailed guidance on how to perform the claimed methods using a variety of starting cell lines, and how to determine whether or not the method was successfully carried out. If the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility," the enablement requirement is met. *See In re Vaeck*, 947 F.2d at 496. Furthermore, "[w]here the specification provides guidance in selecting the operating parameters that would yield the claimed result, it is fair to conclude that the experimentation required to make a particular embodiment is not 'undue'." *PPG Indust.*, 75 F.3d at 1565.

The examiner asserts that the claimed method is not predictable, pointing to the fact that in some of the experiments reported in the Steuer Declaration, a new cell type apparently was not produced. What the examiner fails to recognize, however, is that the two experiments which did not produce a new cell type *were not done in accordance with the claimed methods*, but rather were experiments wherein no aerobic atmosphere was introduced during culture. *See* Final Report (attached to the Robinson Declaration), page 1 "Conclusion," and the discussions of procedures and results at pages 3-6 and 8-9. As such, these two experiments do not prove unpredictability of the procedure. The uncontroverted evidence of record shows that *every experiment* carried out in accordance with the claimed methods produced a new cell type as recited in the claims.

The examiner has failed to provide any evidence that the availability of these cells lines and/or the cited journal article do not enable the claims, and has therefore failed to impeach the

presumptive accuracy of the specification. *In re Marzocchi*, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971); *Fiers v. Revel*, 984 F.2d 1164, 1171-72 (Fed. Cir 1993). In particular, the examiner has

(1) failed to support with substantial evidence within the record his assertion that "there is no reasonable expectation that any and all types of bacteria may be 'produced' or even isolated from any an all cell cultures by the procedure claimed" (October 12, 2005 Office Action, page 11);

(2) failed to support with substantial evidence within the record his assertion that "the specification provides insufficient guidance for one skilled in the art to obtain such [starting] cell cultures (*Id.*);

(3) failed to support with substantial evidence within the record his assertion that "the claimed method is unpredictable and would appear to depend on the type of cell culture and the type of virus employed" (October 12, 2005 Office Action, page 12);

(4) failed to support with substantial evidence within the record his assertion that the present invention "would also require undue experimentation to practice in view of the unpredictable completion of the culturing steps" (*Id.*);

(5) failed to support with substantial evidence within the record his assertion that "retroviral genes have been found to be ubiquitous in all types of different organisms, such that virtually any cell culture would reasonably be expected to have at least pieces of DNA from those viruses" (October 12, 2005 Office Action, page 13); and

(6) failed to support with substantial evidence within the record his assertion that the determination of the presence of viral genes within the cells obtained by the presently claimed methods would require undue experimentation (*Id.*).

Furthermore, the examiner's focus on whether or not any such genes are intact, or integrated into the product cell's genome (Office Action, page 13), is completely beside the point, as there are no such limitations in the claims. Therefore, the presumptive accuracy of the applicant's disclosure stands unimpeached by the evidence. Applicant therefore requests that this rejection be withdrawn.

3. Written description

Claims 24-29 have been rejected under § 112, 1st paragraph, as lacking written description. This rejection is made moot by the cancellation of those claims 24-29. However, to the extent that this rejection might be considered to apply to new claim 31, Applicant provides the following remarks.

The examiner asserts that the claim limitation "not a transgenic cell" is not supported by the specification, and therefore lacks written description. October 12, 2005 Office Action, page 20. As pointed out in the Appeal Brief, this is an improper application of an *in haec verba* standard. A term need not be literally or exactly stated in the specification in order to be described therein. *See, e.g., Purdue Pharma L.P. v. Faulding Inc.*, 56 U.S.P.Q2d 1481, 1483 (Fed. Cir. 2000) (no *in haec verba* test for written description – a limitation need only be conveyed with reasonable clarity). "The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language." *In re Kasloaw*, 217 U.S.P.Q. 1089, 1096 (Fed. Cir. 1983).

As the applicant detailed in his Appeal Brief at pages 23 and 24, the specification as filed clearly states that an aspect of the invention is a method for producing pleiomorphic cells expressing animal and/or viral genes that does not require any step to introduce these genes into the cells from which the pleiomorphic cells are produced. *See, e.g.*, specification page 6, lines 24-30; page 9, lines 5-14; page 10, line 27 to page 11, line 27. The specification as originally filed also describes in detail, in the form of working examples (*e.g.*, Examples 1-5), that such cells are produced without any step that introduces a transgene into the cells. A "transgene" is a gene that is not found in a cell in its natural state, but is rather introduced into a cell, for example by traditional molecular biology transformation techniques, or by recombination with a genomically different cell (for example by bacterial conjugation).[4] "Transgenic" is the adjective used to describe a cell containing a transgene. The specification undeniably describes methods that omit any traditional transformation used in "recombinant" molecular biology techniques that would introduce a transgene, and the cells produced by these methods would therefore *not* be transgenic. As the Board has pointed out, the specification disclosure does establish that the starting cell culture used in the methods therein described (and as now claimed) is free of contamination, as are the cells produced thereby – thus there is no genomically different cell present at the start of the process with which a natural recombination

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[4] See, e.g., Klug & Cummings, *Concepts of Genetics*, 2nd ed. (1983), pages 178-79 and 330-34; Lewin, *Genes V* (1999), page 1256; Dorland's Medical Dictionary (on-line edition), http://www.mercksource.com/pp/us/cns/cns_hl_dorlands.jspzQzpgzEzzSzppdocszSzuszSzcommonzSzdorlandszSzdorlandzSzdmd_t_16zPzhtm, copies of which are attached for the Examiner's convenience.

event could have occurred. Taken as a whole, the disclosure of the specification would be clearly understood by a person having ordinary skill in the art to describe a pleiomorphic cell that is "not transgenic," in addition to the other characteristics recited in the claims. A person having ordinary skill in the art would immediately understand that such cells are "not transgenic," because they do not contain a transgene, and that claim 31 is directed to this embodiment of the invention. The terms "transgene" and "transgenic" have well-established and specific meanings in the art.

For the foregoing reasons, and for the reasons detailed in the applicant's Appeal Brief, Applicant respectfully submits that this rejection, to the extent that it might be applied to new claim 31, would be improper.

B. Rejection under § 112, 2nd paragraph

Claims 1-29 were rejected under 35 U.S.C. § 112, 2nd paragraph as being vague and indefinite. The cancellation of claims 1-3, 15-18, 24- 29 makes this rejection moot with respect to those claims.

The specific rejection of claims 1 and 15 as being vague and indefinite by use of the language "under low oxygen conditions" (October 12, 2005 Office Action, page 20), is moot in view of the cancellation of those claims.

The specific rejection of claims 2, 3 and 15 as being vague and indefinite by use of the term "subjecting the cells to an aerobic culturing step," though they depend upon claims that require culturing under low oxygen conditions (*Id.*), is moot in view of the cancellation of those claims.

Pending claims 4-14 and 19-23, therefore, stand rejected for failing to adequately describe the invention. October 12, 2005 Office Action, pages 20-25. The examiner asserts that the applicant's statements in Paper No. 7, filed June 24, 2000, are evidence that the claims do not correspond in scope to what the applicant regards as his invention. In particular the examiner asserts that the statement by the applicant that "any eukaryotic genes present in bacteria produced by the claimed means would be intact, stable and integrated into the genome, because that would be their condition prior to the performance of the claimed methods" shows that the claims do not correspond in scope to the invention, because the claims recite methods of producing a bacterium containing a single eukaryotic gene, not a bacterium that has the phenotype of a prokaryote and the genotype of a eukaryote. October 12, 2005

Office Action, pages 20-21. Applicant maintains the position set forth in his Appeal Brief that this rejection is improper. As detailed fully in the Appeal Brief at pages 22 and 23, because the claims do not require that there be only a single eukaryotic gene present, or that any gene present be intact, or exclude the presence of an entire, intact genome, the asserted contradiction does not in fact exist. To the extent this statement could be construed to the contrary, Applicant again clarifies his consistent position on this point: the purpose and intention of those statements was to rebut specifically the examiner's assertions at page 9 of the March 22, 2002 Office Action that "it is unclear how one skilled in the art would determine and assure that the actual viral and/or eukaryotic genes are indeed intact genes picked up rather than random fragments thereof," and that "it is unclear whether such pieces are to be stably incorporated into the genome and that proteins will be expressed by them." The examiner's assertion was based on the assumption that eukaryotic genes were "picked up" by contaminating bacteria (now moot in any case in view of the present amendments to the claims requiring sterile conditions throughout the claimed process). The applicant's statement quoted by the examiner was meant to point out the obvious fact that eukaryotic genes present in the cells produced using the claimed method are present as a result of their having been in the starting eukaryotic cell culture. Such genes, of course, would be expected to largely be intact, stable, and integrated into the cell's genome. Applicant will not restate the discussion presented above that the record evidence shows that the cells resulting from the claimed method are not culture contaminants. The Applicant recognizes that the use of the phrase "any eukaryotic genes present" was not a clear use of language, as it could be taken to mean that *every* eukaryotic gene present in the resulting cells would be stable, intact and integrated into the genome, however this statement has been so thoroughly and consistently clarified by the applicant during subsequent prosecution that there can be little doubt as to its intended meaning, and relation to the patentability of the claimed invention. For all of the foregoing reasons, and for the reasons set forth in the applicant's Appeal Brief, the applicant respectfully requests that this rejection be withdrawn with respect to claims 4-14, 19-23 and 27, and that it is not applicable to new claims 30 and 31.

Claims 24 and 25 have been rejected as being rendered vague and indefinite by the use of the terms "derived," "evolved," and "pleiomorphic." October 12, 2005 Office Action, page 21. This rejection is rendered moot by the cancellation of those claims. Applicant maintains, for the reasons detailed in the Appeal Brief at pages 23-24, that claim 24 fully met the requirements of the second paragraph of § 112. However, in the interest of advancing the prosecution, new

claim 31 has been substituted for claim 24. To the extent that this rejection could be applied to new claim 31, that claim recites "a pleiomorphic cell that is identifiable as a bacterium, and contains a eukaryotic and/or viral gene", prepared by a specific series of process steps. The Board has indicated that this language is appropriate language for describing the cells produced by the methods of the invention. Remand, pages 7-9. With regard to the use of the term "pleiomorphic," the examiner asserts, without any evidentiary support, that "all cells are pleiomorphic since they have the ability to alter their shape based on environmental conditions." October 12, 2005 Office Action, page 25. Despite being directed by the Board to support his findings of fact and conclusions of law with "substantial evidence within the record" (Remand, pages 9-10), the examiner provides no evidence that the term "pleiomorphic" has his asserted meaning in the art. In contrast, the applicant has provided evidence which shows that the examiner's asserted definition doe not accord with the ordinary meaning in the art of the term. As the evidence of record shows, the examiner's assertion regarding the scope of the definition is simply incorrect. "Pleiomorphic" does *not* mean simply "the ability to alter shape," based on environmental conditions or otherwise, but rather the ability to assume *distinct forms* (*c.f.*, definition of "pleiomorphic" provided as an attachment to Applicant's Appeal Brief, and the description of pleiomorphic cells reported in the literature as described in the specification at page 3, lines 4-12). The examiner also asserts that the presence of additional claim limitations, "does not lend 'definiteness' to a given term." October 12, 2005 Office Action, page 25. This is a misapplication of § 112, 2nd paragraph, which requires that the *claims* be definite. The fact that one term in a claim may be broad or general (which is not even the case here), the claim language as a whole can indeed define a context in which the meaning of that term is clear and definite, such that the claim as a whole is definite. A common example of this is the use of a "wherein" clause to define a broad claim term. Thus, the examiner cannot simply disregard the presence of claim limitations and focus on a single claim term in isolation, as he has done in this case. The additional limitations in new claim 31, and even those present in original claim 24, provide three firm additional bases which, taken together, clearly distinguish the claimed cells: (1) the cells are not transgenic, (2) they are derived from a eukaryotic cell, and (3) they contain at least one gene evolved from the genome of a eukaryotic cell. New claim 31 also provides additional clear bases for distinguishing the claimed cells: (a) they are identifiable as bacteria, yet (b) contain a eukaryotic and/or viral gene. This language is as clear and distinct as the subject matter allows, and would be readily understood by a person having ordinary skill in the art in the context of the invention, as the Board appears to agree. Applicant therefore submits

that new claim 31 fully meets the requirements of the second paragraph of § 112, and respectfully submits that this rejection is not applicable to that claim.

With regard to the claim terms "derived" and "evolved," these terms have well-established meanings in the art. "Derived" means to get or obtain something from a source,[5] and in the present context unambiguously refers to obtaining a particular cell type (as characterized in the claims), from another cell type (i.e., from a virally-infected eukaryotic cell). In any event, present claim 31 sets out a specific series of steps by which the resulting cell is derived. "Evolved," as the examiner correctly states, means "to develop or arise through the evolutionary process." However, the examiner is incorrect in his assertion that the process is "gradual over time," and in fact the very definition quoted by the examiner does *not* state that evolution means to develop or arise *gradually*. Evolution can be rapid, or sudden, in particular with respect to microbes and other cells placed under altered environmental conditions, as the rapid acquisition of antibiotic resistant by bacteria, for example, shows. It is applied to changes in whole organisms (for example, by speciation), to parts or organs of animals (for example, appendages or coloration), and to single genes (as in the example of antibiotic resistance).[6]

Claim 27 stands rejected as being rendered vague by the use of the term "morphology that is neither prokaryotic nor eukaryotic." Final Office Action, page 15. This rejection is moot in view of the cancellation of this claim.

CONCLUSION

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[5] *See, e.g., Webster's New World College Dictionary*, 4th ed. (copy of the relevant page attached for convenience); Webster's definition of the word as applied in the chemical context is also informative in the present context: "to obtain or produce (a compound) from another compound by replacing one element with one or more other elements."

[6] "evolution ... 5. *Biol. a)* the development of a species, organism, or organ from its original or primitive state to its present or specialized state; phylogeny or ontogeny *b)* Darwinian theory." *Webster's New World Collegiate Dictionary*, 4th ed. "Ontogeny" is "the life cycle of a single organism; biological development of the individual." *Id.* (copies of relevant pages attached for convenience). The encompassment of ontogeny within the definition of evolution in particular shows that the meaning is not reserved for processes that are gradual over time – it is well-established that many organisms develop individually in a matter of days, or even hours.

It is respectfully submitted that the present claims overcome all of the pending rejections, and address all of the points raised by the Board in its Remand, and therefore are in condition for allowance. Favorable action is earnestly requested.

Please note that the correspondence address for this application has been changed and that a supplemental power of attorney and change of address are submitted herewith.

Applicant further requests an interview prior to the next Office Action in this case, in order to expeditiously resolve any issues that might be remaining and, per the Board's directive, advance prosecution.

Respectfully submitted,

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Reg. No. 40,315

Date February 10, 2006